

**PCT**WORLD INTELLECTUAL PROPERTY ORGANIZATION  
International Bureau

## INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

<b>(51) International Patent Classification <sup>7</sup> :</b> <b>A61K 38/21, 31/7056, A61P 31/14</b>	<b>A3</b>	<b>(11) International Publication Number:</b> <b>WO 00/37110</b> <b>(43) International Publication Date:</b> 29 June 2000 (29.06.00)
<b>(21) International Application Number:</b> PCT/US99/27935 <b>(22) International Filing Date:</b> 16 December 1999 (16.12.99) <b>(30) Priority Data:</b> 09/215,876 18 December 1998 (18.12.98) US <b>(71) Applicant:</b> SCHERING CORPORATION [US/US]; 2000 Galloping Hill Road, Kenilworth, NJ 07033 (US). <b>(72) Inventors:</b> GLUE, Paul, W.; 13 Allens Comer Road, Flemington, NJ 08822 (US). ALBRECHT, Janice, K.; 1308 Temple Grove Court, Winter Park, FL 32789 (US). <b>(74) Agents:</b> HOFFMAN, Thomas, D. et al.; Schering-Plough Corporation, Patent Dept. K-6-1 1990, 2000 Galloping Hill Road, Kenilworth, NJ 07033-0530 (US).		<b>(81) Designated States:</b> AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LU, LV, MA, MD, MG, MK, MN, MX, NO, NZ, PL, PT, RO, RU, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UZ, VN, YU, ZA, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).  <b>Published</b> <i>With international search report.</i>  <b>(88) Date of publication of the international search report:</b> 14 September 2000 (14.09.00)
<b>(54) Title:</b> RIBAVIRIN-PEGYLATED INTERFERON ALFA INDUCTION HCV COMBINATION THERAPY  <b>(57) Abstract</b>  The use of ribavirin and interferon alpha for the manufacture of pharmaceutical compositions for treating a patient having chronic hepatitis C infection, e.g., a patient having HCV genotype 1, 2 or 3, to eradicate detectable HCV-RNA by a method comprising administering an effective amount of ribavirin in association with an effective amount of pegylated interferon alpha, characterised in that treating patients having chronic hepatitis C infections is effected in two treatment time periods: (a) a first treatment time period of at least 20 to 30 wherein a therapeutically effective amount of ribavirin and a therapeutically effective induction dosing amount of pegylated interferon-alfa, e.g., pegylated interferon-alfa-2b sufficient to at least substantially lower, and preferably to eradicate, detectable HCV-RNA, are administered; and (b) a second treatment time period of at least 20 to 30 weeks wherein a therapeutically effective amount of ribavirin and a therapeutically effective amount of pegylated interferon-alfa are administered sufficient to maintain no detectable HCV-RNA for at least 20-30 weeks are administered after the end of the first treatment time period and to maintain no detectable HCV-RNA for at least 24 weeks after the end of the second treatment time period is disclosed.		

**FOR THE PURPOSES OF INFORMATION ONLY**

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AL	Albania	ES	Spain	LS	Lesotho	SI	Slovenia
AM	Armenia	FI	Finland	LT	Lithuania	SK	Slovakia
AT	Austria	FR	France	LU	Luxembourg	SN	Senegal
AU	Australia	GA	Gabon	LV	Latvia	SZ	Swaziland
AZ	Azerbaijan	GB	United Kingdom	MC	Monaco	TD	Chad
BA	Bosnia and Herzegovina	GE	Georgia	MD	Republic of Moldova	TG	Togo
BB	Barbados	GH	Ghana	MG	Madagascar	TJ	Tajikistan
BE	Belgium	GN	Guinea	MK	The former Yugoslav Republic of Macedonia	TM	Turkmenistan
BF	Burkina Faso	GR	Greece			TR	Turkey
BG	Bulgaria	HU	Hungary	ML	Mali	TT	Trinidad and Tobago
BJ	Benin	IE	Ireland	MN	Mongolia	UA	Ukraine
BR	Brazil	IL	Israel	MR	Mauritania	UG	Uganda
BY	Belarus	IS	Iceland	MW	Malawi	US	United States of America
CA	Canada	IT	Italy	MX	Mexico	UZ	Uzbekistan
CF	Central African Republic	JP	Japan	NE	Niger	VN	Viet Nam
CG	Congo	KE	Kenya	NL	Netherlands	YU	Yugoslavia
CH	Switzerland	KG	Kyrgyzstan	NO	Norway	ZW	Zimbabwe
CI	Côte d'Ivoire	KP	Democratic People's Republic of Korea	NZ	New Zealand		
CM	Cameroon			PL	Poland		
CN	China	KR	Republic of Korea	PT	Portugal		
CU	Cuba	KZ	Kazakhstan	RO	Romania		
CZ	Czech Republic	LC	Saint Lucia	RU	Russian Federation		
DE	Germany	LI	Liechtenstein	SD	Sudan		
DK	Denmark	LK	Sri Lanka	SE	Sweden		
EE	Estonia	LR	Liberia	SG	Singapore		

# INTERNATIONAL SEARCH REPORT

International Application No.

PCT/US 99/27935

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 A61K38/21 A61K31/7056 A61P31/14

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P, X	P. GLUE ET AL.: "A DOSE-RANGING STUDY OF PEG-INTRON AND RIBAVIRIN IN CHRONIC HEPATITIS C. SAFETY, EFFICACY AND VIROLOGIC RATIONALE" HEPATOLOGY (SUPPLEMENT), vol. 30, no. 4(2), October 1999 (1999-10), page 303A XP002138613 USA abstract -/-	1-25

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

### \* Special categories of cited documents:

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance: the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance: the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search

25 May 2000

Date of mailing of the international search report

28/06/2000

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2  
NL - 2280 HV Rijswijk  
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,  
Fax (+31-70) 340-3016

Authorized officer

Economou, D

## INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 99/27935

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No. --
P, X	M.SULKOWSKI ET AL.: "COMBINATION THERAPY WITH PEGINTERFERON ALPHA-2A (PEG-IFN) AND RIBAVIRIN IN THE TREATMENT OF PATIENTS WITH CHRONIC HEPATITIS C (CHC)" HEPATOLOGY (SUPPLEMENT), vol. 30, no. 4(2), October 1999 (1999-10), page 197A XP002138614 USA abstract	1-25
P, X	JAYANT TALWALKAR ET AL.: "COMBINATION THERAPY WITH INTERFERON-ALFA-2B (INTRON-A) AND RIBAVIRIN (REBETOL) IN CHRONIC HEPATITIS C PATIENTS PREVIOUSLY RELAPSING OR NOT RESPONDING TO INTERFERON" HEPATOLOGY (SUPPLEMENT), vol. 30, no. 4(2), October 1999 (1999-10), page 197A XP002138615 USA abstract	1-25
P, X	ALGRANATI N.E. ET AL.: "A BRANCHED METHOXY 40 KDA POLYETHYLENE GLYCOL (PEG) MOIETY OPTIMIZES THE PHARMACOKINETICS (PK) OF PEGINTERFERON ALPHA-2A (PEG-IFN) AND MAY EXPLAIN ITS ENHANCED EFFICACY IN CHRONIC HEPATITIS" HEPATOLOGY (SUPPLEMENT), vol. 30, no. 4(2), October 1999 (1999-10), page 190A XP002138616 USA abstract	1-25
P, X	MITCHELL SCHIFFMAN MITCHELL ET AL.: "CONTROLLED, RANDOMIZED, MULTICENTER, DESCENDING DOSE PHASE II TRIAL OF PEGYLATED INTERFERON ALPHA-2A (PEG) VS STANDARD INTERFERON ALPHA-2A (IFN) FOR TREATMENT OF CHRONIC HEPATITIS C" GASTROENTEROLOGY, vol. 116, no. 4(2), April 1999 (1999-04), page 1275 XP002138617 USA abstract	1-25
P, X	EP 0 956 861 A (SCHERING CORPORATION) 17 November 1999 (1999-11-17) the whole document claims 1-12	1-25
P, X	EP 0 903 148 A (SCHERING CORPORATION) 24 March 1999 (1999-03-24) the whole document claims 1-18	1-25